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Generic Inhibition of the Selected Movement and Constrained Inhibition of Nonselected Movements during Response Preparation

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Abstract

Previous studies have identified two inhibitory mechanisms that operate during action selection and preparation. One mechanism, competition resolution, is manifest in the inhibition of the nonselected response and attributed to competition between candidate actions. The second mechanism, impulse control, is manifest in the inhibition of the selected response and is presumably invoked to prevent premature response. To identify constraints on the operation of these two inhibitory mechanisms, we manipulated the effectors used for the response alternatives, measuring changes in corticospinal excitability with motor-evoked potentials to TMS. Inhibition of the selected response (impulse control) was independent of the task context, consistent with a model in which this form of inhibition is automatically triggered as part of response preparation. In contrast, inhibition of the nonselected response (competition resolution) was context-dependent. Inhibition of the nonselected response was observed when the response alternatives involved movements of the upper limbs but was absent when one response alternative involved an upper limb and the other involved a lower limb. Interestingly, competition resolution for pairs of upper limbs did not require homologous effectors, observed when a left index finger response was pitted with either a nonhomologous right index finger movement or a right arm movement. These results argue against models in which competition resolution is viewed as a generic or fully flexible process, as well as models based on strong anatomical constraints. Rather, they are consistent with models in which inhibition for action selection is constrained by the similarity between the potential responses, perhaps reflecting an experience-dependent mechanism sensitive to the past history of competitive interactions.

INTRODUCTION

Action selection entails a decision process that requires the actor to make a choice between potential actions and the movements required to achieve those actions (Cisek & Kalaska, 2010; Gold & Shadlen, 2007). Such choices have been characterized as a competitive process between response options, whereby selection is facilitated by the accumulation of evidence favoring selection of each candidate as well as inhibition of nonselected options. In this article, we investigate constraints on the latter, examining the conditions under which inhibitory interactions between candidate actions are manifest.

TMS has provided a tool to assess the dynamics of corticospinal (CS) excitability during action selection and response initiation. Before movement onset, there is a graded increase in the motor-evoked potentials (MEPs) elicited in agonist muscles following M1 TMS (Leocani, Cohen, Wassermann, Ikoma, & Hallett, 2000; MacKinnon & Rothwell, 2000). Surprisingly, in delay tasks in which a cue indicates the forthcoming response, the MEPs in the agonist are severely attenuated, an effect that has been termed impulse control (IC; Duque & Ivry, 2009). This inhibition of the selected response may help ensure that the response is not emitted before the presentation of an imperative signal (Duque, Lew, Mazzocchio, Olivier, & Ivry, 2010). Inhibition is also observed in the agonist for the nonselected response during the delay period, an effect that remains present after the imperative signal (Duque et al., 2010). This inhibition has been termed competition resolution (CR), assumed to reflect the operation of processes that sharpen selection. Various lines of evidence support the idea that IC and CR reflect two distinct forms of inhibition that operate during action selection (Duque, Labruna, Verset, Olivier, & Ivry, 2012), including evidence that IC is evident at the spinal level (Prut & Fetz, 1999; Touge, Taylor, & Rothwell, 1998) whereas CR is restricted to more central representations (Duque et al., 2010).

These two inhibitory mechanisms place different computational demands on selection and preparatory processes. IC is hypothesized to reflect the gating of a planned action, keeping the response in check until the presentation of the imperative signal. As such, IC is a self-inhibitory process, with the activation of the response assumed to trigger downstream inhibition specific to that response. In contrast, the computational requirements for CR would appear to be more complex. In the most generic form of control, the activation of one response might entail the inhibition of all other responses. Alternatively, CR might operate in a more limited manner, restricted to interactions between task-relevant response alternatives or constrained by anatomical factors such as inhibitory connections between homologous effectors.

In the present experiments, we manipulated the relationship between the response alternatives to identify constraints on preparatory inhibition in action selection. Experiment 1 was designed to test the ubiquity of IC and CR. We compared two conditions in which the pair of responses either involved homologous movements (index finger abduction) or highly distinct movements (left finger abduction vs. right foot adduction). The main dependent variable of interest was the change in excitability during the preparatory period of the first dorsal interosseous muscle (FDI) of the left hand, the agonist for the left hand movement. We predicted that IC would be invariant across conditions, reflecting the fact that it operates on the selected response, independent of the relationship of this response to the non-selected alternative. Our predictions for CR were more open-ended. If CR reflects the operation of a generic process, we would expect to observe similar inhibition of the left hand when the selected response involved a finger or foot movement. Alternatively, if CR operates in a more specific manner, then we expected to observe greater inhibition in the condition involving homologous response alternatives. Competitive interhemispheric interactions reflecting the mirror organization of the motor system have been observed in many behavioral and physiological studies (Diedrichsen, Wiestler, & Krakauer, 2013; Sattler, Dickler, Michaud, & Simonetta-Moreau, 2012; Hinder, Schmidt, Garry, & Summers, 2010). As such, competition is likely to be related to the degree of similarity between the response alternatives.

As described below, the results of Experiment 1 showed that CR was only evident in the condition in which the response alternatives were homologous, at odds with the hypothesis that CR is a generic process. To further explore constraints on this process, we conducted a second experiment in which neither response pairing involved homologous muscles. In one

condition, the left and right hand responses involved the same effector (index finger), but the responses were asymmetrical. In the other, a left hand finger response was paired with a right arm movement. If interhemispheric competition is restricted to interactions between homologous muscles, we would expect to not observe CR in either condition. Alternatively, the degree of competition might reflect the functional overlap between the response alternatives; for example, CR might be modulated by the likelihood that different response alternatives are in competition in natural behavior.

METHODS

Participants

Twenty-three healthy participants participated in the two experiments (Experiment 1: $n = 12$: 6 women and 6 men; 21 ± 1.8 years old; Experiment 2: $n = 11$: 7 women and 4 men; 21 ± 1.8 years old). As assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), 20 participants were right-handed and 3 were left-handed. In previous studies, we have not observed differences in IC and CR as a function of handedness.

All participants were naive to the purpose of the study and were financially compensated. The protocol was approved by the institutional review board at University of California, Berkeley, with written consent obtained before the start of the experiment.

TMS

TMS was delivered through a 70-mm, figure-of-eight coil driven by a Magstim 200 magnetic stimulator (Magstim, Whitland, Dyfed, UK). To measure CS excitability, MEPs were elicited in a left hand muscle by TMS stimulation over the right motor cortex in all participants. The coil was placed tangentially on the scalp with the handle oriented toward the back of the head and laterally at a 45° angle from the midline, an orientation that is approximately perpendicular to the central sulcus. The targeted muscle was always the left FDI, the agonist for index finger abduction.

For the experimental session, the intensity of TMS was set to 115% of resting motor threshold (rMT), defined on an individual basis. We first identified the optimal spot for eliciting MEPs in the targeted muscle and then marked that position on the participant's scalp to provide a reference point throughout the experimental sessions. The rMT was defined as the minimal TMS intensity required to evoke MEPs of $\sim 50 \mu\text{V}$ peak-to-peak amplitude in the targeted muscle on 5 of 10 consecutive trials (Rossini et al., 1994). The mean rMT for FDI corresponded to 41% ($SD = 7.6$) and 46% ($SD = 9.4$) of maximum stimulator output in Experiments 1 and 2, respectively.

EMG Recording

EMG was recorded from surface electrodes placed over the agonist muscles for the task-relevant movements for each experiment (see below). In Experiment 1, the agonists were left FDI, paired with either right FDI or right tibialis anterior. In Experiment 2, the agonists were left FDI, paired with right extensor indicis or the short head of the right biceps brachii. The EMG signal was monitored on-line to ensure that participants maintained a relaxed posture over the course of the experiment. The EMG signals were amplified and bandpass-filtered on-line between 50 and 2000 Hz (Delsys, Inc.). The signals were digitized at 2000 Hz for off-line analysis. EMG data were collected for 3 sec on each trial, starting 200 msec before the TMS pulse.

Procedure

Participants sat in front of a computer screen with both hands resting on a pillow, palms down, with the arms in a semiflexed position, and their feet flat on the floor.

We used a delayed-response, choice RT task to examine changes in CS excitability during response preparation (Duque & Ivry, 2009). Participants were informed that they would play a virtual “soccer game” in which the required response was indicated by the orientation of the goal and position of the “ball” (see Figure 1, left side). Each trial began with the brief presentation (100 msec) of a cross at the center of the screen, followed 600 msec later by a preparatory cue. This cue consisted of a bracket (the soccer goal) positioned in the center of the screen, with the open side facing toward the left or right side. The orientation of the bracket indicated the forthcoming response. When the open side faced to the left, the response would be made with the task-relevant effector from the left side of the body; when the open side faced right, the response would be made with the task-relevant effector from the right side of the body. After a 900-msec preparatory interval, a filled circle (the soccer ball) appeared. This served as the imperative to the participant to initiate the cued response. The participant was instructed to prepare the response during the delay period so that they could respond as quickly as possible following the imperative signal. To promote fast responses, the imperative only remained visible for 300 msec. To prevent the participant from anticipating the imperative, we included “catch trials” in which an “X” appeared in the middle of the screen at the time of the imperative. The participant was instructed to not respond.

Each experiment tested two conditions, with the difference between the conditions based on the combination of effectors (Figure 1, right side). Each condition was repeated twice, such that the test session consisted of four blocks of trials. The order of blocks was counterbalanced across participants. There were 80 trials per block, 35 for each response (left or right effectors) and 10 catch trials, with the order of trials randomized. In each experiment, participants started with a practice block of 30 trials, 15 for each condition.

Within each block, TMS was applied on 60 of the 80 trials. The TMS pulse was applied at one of two intervals. Twenty “baseline measurements” were obtained during each block by applying the TMS pulse synchronously with the onset of the fixation cross (baseline trials). Forty “delay measurements” were obtained by applying the TMS pulse during the delay period, 800 msec after the onset of the cue (100 msec before the onset of the imperative). Of these 40, 20 were obtained in which the targeted muscle was the agonist for the selected response (selected trials) and 20 in which the targeted muscle was the agonist for the nonselected response (nonselected trials). The inclusion of 20 no-TMS trials per block prevented the participants from anticipating the pulse and also provided trials in which we could measure RT in the absence of TMS. These no-TMS trials randomly occurred on both regular and catch trials. Each block lasted approximately 7 min, and the entire experimental session lasted approximately 60 min.

Experiment 1

We compared one condition in which the two responses involved homologous muscles to a second condition in which the two responses involved nonhomologous muscles. In a “Finger–Finger_{homolog}” condition, the participants were instructed to “shoot the ball into the goal” by abducting either the left or right index finger. In a “Finger–Foot” condition, the responses required either abduction of the left index finger or adduction of the right foot. We used this pairing so that the direction of movement for each effector was toward the midline of the body. From the initial posture, foot abduction required that the participant slightly lift the foot, a movement for which the tibialis anterior is the agonist. MEPs were always

recorded from the left FDI. Thus, this muscle was considered “selected” for left hand responses and “nonselected” for right hand or foot responses.

Experiment 2

In Experiment 2, we compared two conditions, neither of which involved a choice between homologous muscles. In both conditions, the left hand response was as in Experiment 1, abduction of the left index finger. In the “Finger–Finger_{nonhomolog}” condition of Experiment 2, the right hand response required extension of the right index finger and the participant was instructed to “shoot the ball above the goal” (Finger–Finger_{nonhomolog}). In the “Finger–Arm” condition, the right limb response required flexion of the right elbow. Note that in the Finger–Finger_{nonhomolog} condition, the two movements involved the same effector, but the directions of the two responses were not symmetric, and the experimenter-defined goal was non-identical. In the Finger–Arm condition, the two movements were roughly symmetric toward the midline of the body, designed to achieve a common goal, but involved nonhomologous effectors. As in Experiment 1, MEPs were always recorded in left FDI.

Data Analysis

All dependent variables were based on the EMG data. RT was defined as the time interval between the onset of the imperative signal and an increase in EMG activity of the agonist muscle. The RT of the volitional response was easily identified with an interactive program in which the EMG increase was visually identified and marked. MEPs were recorded from the left FDI channel, defined as the peak-to-peak change in amplitude of the EMG signal. To prevent contamination of the MEP measurements by fluctuations in background EMG, we excluded trials in which the background EMG (EMG_{RMS}: root mean square) activity was greater than 0.01 mV in the 200-msec window preceding the TMS pulse (Duque & Ivry, 2009; Duque et al., 2005, 2007). We also excluded MEPs that were above or below 3 *SD* of the mean MEP amplitude for that condition. After trimming the data for errors (EMG increases in the muscle for the noncued response) and trials in which the MEP data did not meet our inclusion criteria, an average of 38 MEPs were included in the analysis of individual participants (out of a maximum of 40) for each measure of IC and CR.

To assess changes in CS excitability during response preparation, mean MEP values were obtained for each participant on baseline trials, selected trials, and non-selected trials. The data were averaged over the two blocks for a given condition. To normalize the MEP data, the mean MEP values obtained during the delay period were divided by the mean baseline MEP, with the latter combined for selected and nonselected trials. This ratio served as a measure of IC when the numerator was based on MEPs from trials in which the targeted muscle was selected. The ratio provided a measure of CR when the numerator was from trials in which the same muscle was non-selected. Note that separate baseline measures were used for the two conditions within an experiment (Labruna, Fernandez-del-Olmo, & Ivry, 2011).

We performed two analyses of the RT data. A first analysis was restricted to the no-TMS trials and involved a two-way repeated-measure ANOVA with the factors Condition (e.g., Experiment 1: Finger–Finger_{homolog}, Finger–Foot) and Response Side (Left, Right). To assess the effects of TMS on RT, we used a three-way ANOVA, including the factor Stimulation Epoch (None, Baseline, Delay). The normalized MEP data were evaluated in a two-way repeated-measure ANOVA with the factors Condition (e.g., Experiment 1: Finger–Finger_{homolog}, Finger–Foot) and Cue (Selected, Nonselected). Post hoc comparisons were conducted using the Fisher's least significant difference (LSD) procedure. For the MEP data, paired *t* tests were used to evaluate if the change in excitability during the delay period was significantly different from baseline.

RESULTS

Experiment 1

RT—Collapsed across the two conditions, the mean (EMG-defined) RT on no-TMS trials was 258 msec for responses with the left index and 260 and 261 msec for responses with the right index finger or right foot, respectively (Table 1). In an ANOVA restricted to these trials, RT did not vary as a function of Condition, $F(1, 11) = 0.29, p = .60$, Response Side, $F(1, 11) = 0.16, p = .70$, nor did these factors interact, $F(1, 11) = 0.31, p = .59$. Although we did not include a no-cue condition, these RTs are fast for a go-no-go (catch trials) task, consistent with the assumption that the participants followed the instructions to use the cue to prepare their responses.

RTs were faster on TMS trials. When the pulse occurred at the start of the trial (baseline), the mean RT was 238 msec for the left hand and 231 and 251 msec for responses with the right hand or right foot, respectively. RTs were even faster when the pulse occurred just before the imperative signal (delay: left hand = 223 msec; right hand = 226 msec; right foot = 223 msec). These differences were confirmed in an ANOVA showing that RT varied as a function of the epoch in which the TMS pulse was applied, $F(2, 22) = 6.15, p = .008$. Post hoc tests revealed that RTs on no-TMS trials were marginally slower compared with trials in which TMS was applied at baseline ($t_{11} = 1.95, p = .077$) and significantly slower when TMS was applied during the delay period ($t_{11} = 5.15, p < .001$). The difference in RT between the trials in which TMS was applied at baseline or during the delay was not reliable ($t_{11} = 1.25, p = .239$). The hastening of RTs on TMS trials is likely because of an alerting effect associated with the sound and/or tactile sensation coming from TMS pulse, rather than effects on CS excitability because it was observed for both left- and right-sided responses.

CS Excitability—We first verified that the MEPs remained stable across conditions. For left FDI, the mean MEP values during the baseline period were 1.84 mV ($SE = 0.36$) and 1.83 mV ($SE = 0.35$) for the Finger–Finger_{homolog} and Finger–Foot conditions, respectively ($t_{11} = 0.15, p = .89$).

We then asked if the MEPs were differentially modulated during the task, relative to baseline, in an ANOVA involving the factors Condition (Finger–Finger_{homolog}/Finger–Foot) and Cue (Selected/Nonselected). The main effects of Condition, $F(1, 11) = 13.39, p = .004$, and Cue, $F(1, 11) = 30.89, p < .0001$, were significant, as was the interaction of these two factors, $F(1, 11) = 14.82, p = .003$. As can be seen in Figure 2A, MEPs were strongly attenuated for the Finger–Finger_{homolog} pairing regardless of whether the effector was selected or not selected for the forthcoming response (compared with baseline value of 100%, both $ps < .001$). A post hoc comparison revealed that the degree of attenuation was greater when the left finger was selected compared with when it was not selected ($t_{11} = 2.71, p = .02$). These results replicate previous findings (Duque et al., 2010; Duque & Ivry, 2009), showing that, when the two response alternatives involved homologous effectors, MEPs are always dramatically attenuated before the imperative and that inhibition of the selected effector (IC) is larger than inhibition of the nonselected effector (CR).

A different picture emerged for the Finger–Foot pairing. Here we also observed IC, with lower MEPS relative to baseline when the left FDI was the agonist for the forthcoming response ($p < .001$). However, the MEP attenuation was markedly reduced when the left FDI was not selected, and relative to baseline, the inhibition was not significant ($p = .28$). Thus, the results from the Finger–Foot condition show that IC was still present when the response alternatives involve nonhomologous effectors, but CR was abolished. This conclusion is further supported by a post hoc comparison of the two nonselected conditions: Mean MEP values were lower in the Finger–Finger_{homolog} condition compared with the

Finger–Foot condition ($p = .001$). A similar comparison of the MEPs for the two conditions in which the left index finger was the selected response showed no difference ($p = .95$).

In summary, the results of Experiment 1 confirmed prior findings that CS excitability is significantly attenuated during the delay period. However, the results provide novel evidence that distinct inhibitory mechanisms are operative on trials in which the targeted effector has been selected or not selected for the forthcoming response as well as identify important constraints on these mechanisms. When the muscle is the agonist for the forthcoming response, the degree of inhibition was relatively invariant. This is consistent with the hypothesis that IC involves an insulated, self-inhibitory process in which preparing a delayed response entails the engagement of an inhibitory mechanism that helps prevent the premature initiation of that response.

In contrast, when the effector was not selected, inhibition was evident in the Finger–Finger_{homolog} condition, but not in the Finger–Foot condition. Thus, CR is not a general feature of response preparation but occurs only under certain conditions. This result argues against a generic model in which reciprocal inhibitory links can be established in an arbitrary manner for any set of response alternatives. The results are also inconsistent with a model in which CR is generated in a self-inhibitory manner, similar to that proposed for IC. If inhibition was the flip side of response-specific activation processes (e.g., “Don’t Move”), then we should have observed it in both conditions.

As in previous studies (Duque et al., 2010; Duque & Ivry, 2009), CR was observed in a condition in which the response alternatives involved left and right index finger movements. The competition between homologous muscles could arise from anatomical and/or functional considerations given the mirror organization of the motor system. However, it is important to first assess whether there is something unique about homologous effectors or whether CR will also be observed with other pairings of left and right effectors. We address this issue in the second experiment.

Experiment 2

RT—As in Experiment 1, RTs were faster on trials in which a TMS pulse was delivered (Effect of Stimulation Epoch: $F(2, 20) = 5.16, p = .016$). Collapsed across conditions, the mean RT on no-TMS trials was 260 msec. On TMS trials, mean RT was reduced to 240 msec when the pulse was applied during baseline and 224 msec when the pulse was applied during the delay period. Post hoc tests revealed that RTs during no-TMS trials were reliably slower compared with trials in which TMS was applied during baseline ($t_{10} = 4.19, p = .002$) or the delay period ($t_{10} = 2.88, p = .016$). The baseline and delay epochs did not differ ($t_{10} = 0.25, p = .81$).

On the no-TMS trials (Table 1), RT did not vary as a function of Condition, $F(1, 10) = 2.44, p = .15$, Response Side, $F(1, 10) = 1.59, p = .24$, nor did these factors interact, $F(1, 10) = 1.45, p = .26$. These two factors were also not reliable in the TMS trials (Condition: $F(1, 10) = 3.63, p = .09$; Response Side: $F(1, 10) = .06, p = .81$), but the interaction was significant, $F(1, 10) = 6.96, p = .025$. In the Finger–Finger_{nonhomolog} condition, RTs were faster ($t_{10} = 4.34, p = .001$) when the response was made with the right hand compared with the left hand. This right–left difference was not found in the Finger–Arm condition ($t_{10} = 1.02, p = .331$).

CS Excitability—The baseline MEPs were comparable across the two conditions. For left FDI, the mean MEP values during the baseline period were 1.18 mV ($SE = 0.26$) for the condition involving a choice between nonhomologous movements of the two index fingers (Finger–Finger_{nonhomolog}) and 1.39 mV ($SE = 0.36$) for the condition involving a choice

between the left index finger and right arm (Finger–Arm). These values were not significantly different from one another ($t_{10} = 1.54$, $p = .15$).

An ANOVA designed to assess if the MEPs were differentially modulated during task performance in the two conditions revealed a main effect of Cue, $F(1, 10) = 16.35$, $p = .002$ (Figure 2B). The degree of inhibition in left FDI was greater on trials in which this muscle was the agonist for the forthcoming response (IC) compared with when it was the agonist for the nonselected response (CR). Thus, the results demonstrate the ubiquitous nature of inhibition targeted at the selected effector during a delay and are consistent with previous findings showing that inhibition associated with IC tends to be larger than inhibition associated with CR.

Our main focus here is on inhibition of left FDI when this muscle is associated with the nonselected response. When compared with baseline, left FDI MEPs were reliably attenuated during the delay period on nonselected trials. This inhibition was observed in both the Finger–Finger_{nonhomolog} condition and Finger–Arm conditions (both $ps = .002$). The effect was similar for the two conditions as revealed in the fact that neither the main effect of Condition, $F(1, 10) = 0.01$, $p = .94$, nor the interaction (Condition \times Cue: $F(1, 10) = 0.03$, $p = .87$) were significant in the ANOVA. In summary, the results of Experiment 2 demonstrate that inhibition of the nonselected response is not restricted to conditions in which the response alternatives involve homologous muscles.

We note that the baseline MEPs were lower in Experiment 2 (mean = 1.29 mV) compared with Experiment 1 (mean = 1.84 mV), although a post hoc between experiment comparison indicated that this difference was not reliable, $F(1, 21) = 1.32$, $p = .263$. There is considerable variability in baseline MEPs, due in part to the relatively sparse data set obtained to determine the rMT. Nonetheless, this variability should have minimal impact on the estimates of IC and CR given that each is calculated as a percentage change from baseline on an individual basis.

DISCUSSION

Behavior entails a constant competition between the possible actions that the environment presents, according to our current goals. Although the decision-making literature has generally focused on choices between objects (e.g., orange juice or apple juice), there has been growing interest in action-based choices (Rangel & Hare, 2010). These choices are usually viewed as emerging from a competitive process involving interactions between potential responses (see Cisek & Kalaska, 2010). TMS has provided an important tool to probe the dynamics underlying action selection and preparation, with prior work having established the existence of two distinct inhibitory mechanisms (Duque et al., 2010; Duque & Ivry, 2009), one associated with determining which response to make and the other with regulating the initiation of the selected response. The current pair of experiments specifies important constraints on the operation of these two mechanisms.

Robustness of Inhibition Arising from IC

Our earlier work had revealed the seemingly, counterintuitive inhibition of the selected response during a delay period. This inhibition is quite pronounced, with MEPs being attenuated by approximately 40–50% from baseline. This inhibition arises although the cortical representation of that response exhibits increased excitability (Duque & Ivry, 2009; Davranche et al., 2007), suggesting a downstream locus of operation. Consistent with this hypothesis, spinal reflexes in the selected response are attenuated (Duque et al., 2010). This pattern of results suggests that IC provides a mechanism to inhibit a response in the face of on-going preparation.

In the current pair of experiments, IC was unaffected by the task context. It was of similar magnitude when the response choices involved homologous muscles, nonhomologous muscles of the same effectors, or nonhomologous muscles of different effectors that were either both in the upper limbs or upper and lower limbs. It is important to note that this inhibition is not generic: When the targeted muscle is unlikely to be selected (task-irrelevant), CS excitability does not change during the delay period (Duque et al., 2010).

The ubiquitous nature of IC suggests that this form of inhibition may be intrinsically part of preparatory processes, at least for delayed response tasks. We envision a self-contained process, involving an architecture where the activation of a response representation automatically triggers a corresponding inhibitory tag, with the latter signal providing a gate on descending signals. Functionally, such inhibition could allow preparatory processes to operate upstream without generating or triggering premature movement. Alternatively, it is possible that downstream inhibition serves to facilitate fast response initiation by lowering background activity at the expected time of the imperative (Hasbroucq, Kaneko, Akamatsu, & Possamai, 1997). Further research is needed to clarify this issue. The current literature does not provide a clear picture as to whether IC is also present in tasks in which there is no delay period.

Most relevant for our current discussion is that this model entails minimal computational requirements on the control system given that IC is linked to response activation. The self-contained nature of the model avoids the need to postulate a control process that regulates the target of inhibition. Although we focus on computational requirements here, various lines of evidence (Duque et al., 2012; Seki & Fetz, 2012) suggest that premotor cortex may be a critical node in a network for triggering the parallel activation of response-specific activation (feeding into motor cortex) and inhibition (targeted downstream of motor cortex; Cohen, Sherman, Zinger, Perlmutter, & Prut, 2010; Kroeger et al., 2010).

Constraints on Inhibition Arising from CR

A priori, we can envision many architectures that could result in inhibition of the nonselected response. Competitive interactions are a common feature in neural networks, invoked to account for operations ranging from low-level sensory processes (e.g., center-surround mechanisms) to high-level processes such as those seen in selective attention tasks (Keitel, Andersen, Quigley, & Muller, 2012; McMains & Kastner, 2011; Desimone & Duncan, 1995). We sketch below a series of models that could underlie CR, asking how they fare in the context of the current results (see Figure 3).

Although the phrase “competition resolution” suggests a competitive process, it is possible that CR might also entail an insulated process (“Self-contained,” Figure 3A), similar to that postulated for IC. In the same manner that we assume a cue triggers the activation of the selected response, a cue specifying another response might trigger inhibition directed at the nonselected response (Anderson & Green, 2001). In this view, a cue could trigger response-specific excitatory signals (“Prepare to Move”) or response-specific inhibitory signals (“Don't Move”). An appealing feature of this model is that, similar to our model of IC, the control of CR is “dumb,” entirely self-contained within the processes associated with each action representation.

At the other extreme, CR might entail a highly distributed form of control where the activation of one response has the capability to inhibit all other potential, task-relevant responses (“Smart,” Figure 3B). Generic inhibition has been reported in studies with the stop-signal task, although in this context, inhibition is evident not only in task-relevant muscles but also in task-irrelevant muscles (Cai, Oldenkamp, & Aron, 2012; Badry et al., 2009). An architecture in which excitation of one response produces inhibition of all other

responses would seem implausible if the inhibitory signals are linked to effector-specific representations. Anatomically, it would be hard to envision an architecture where there were links between all possible responses given the near-infinite set of actions and movements we are capable of producing. Alternatively, one might envision a flexible system in which transient representations of task-relevant actions interact in a competitive manner (Badre, Kayser, & D'Esposito, 2010). By this view, inhibitory links are created in an on-line manner between the response alternatives.

Importantly, the results of Experiment 1 rule out the “self-contained” and fully distributed “smart” models. Both models would predict that CR should be evident independent of task context. However, we did not observe inhibition of the nonselected response in the Finger–Foot condition, although IC remained as robust here as when the choice involved homologous effectors. The selectivity of CR is at odds with the idea that this form of inhibition is generated in a self-inhibitory manner, arguing instead that it involves competitive interactions between response alternatives. However, these interactions are not generic, present for any set of response alternatives.

The selective manifestation of CR in Experiment 1 led us to consider another model, one in which inhibition for CR is limited to interactions between movements involving homologous effectors (“Homologous,” Figure 3C). This hypothesis is further motivated by computational models in which response selection is viewed as an independent race between possible actions, without postulating competitive interactions between the candidates (Brown & Heathcote, 2008). By this view, CR would be viewed as more of the exception, rather than the rule, limited to conditions in which evolution has provided the anatomical basis for inhibitory interactions of different response representations. Indeed, the presence of mirror movements in young children (Koerte et al., 2010; Garvey et al., 2003) and the suppression of these with maturation (de Boer, Peper, & Beek, 2012; Mayston, Harrison, & Stephens, 1999) could be seen as indicative of a mechanisms that might place an anatomical constraint on CR.

The results of Experiment 2, however, clearly argue against this hypothesis since CR was not limited to choices between homologous muscles. Pronounced inhibition of the nonselected response was observed when the choice involved nonhomologous movements. A within-experiment comparison showed that CR was similar when the choice involved different gestures with the same left and right hand effector (index finger) or between different effectors (left finger–right arm).

Given the challenges to the architectures described above, we propose that the constraints on CR may be a function of response similarity. As depicted in Figure 3D (“Proximity/History Dependent”), this form of constraint could reflect both anatomical and functional factors. Anatomically, although CR was not present when the response pairing a mixture of upper and lower limb effectors, CR was present for response pairings between upper limb effectors. Moreover, at least in terms of mean values, inhibition of the nonselected response was greatest when the pair involved homologous effectors (58% of baseline) and weaker when the pair involved nonhomologous effectors (68% for the nonhomologous finger–finger and finger–arm pairings). Although a post hoc, between-experiment comparison of these conditions was not reliable ($p = .35$), the pattern is consistent with the idea that the extent of CR is a function of response similarity, perhaps even related to the proximity of neural representation in a motor homunculus (van den Heuvel & Hulshoff Pol, 2010).

Functionally, constraints on CR may be “experience dependent,” reflecting the degree to which a pair of response options has engaged in prior competitions. By this model, we would expect to observe stronger CR between pairs of responses that are frequently viable

alternatives compared with response pairs that are infrequently pitted against one another. We frequently face situations in which a common goal—to pick up a glass or press the elevator call button—can be performed with either hand. Experience in such flexible contexts could have led to the establishment of reciprocal inhibitory links between the two arms or two fingers. In contrast, we rarely face situations in which the choice for a volitional response is between an upper and lower limb. Although we can interact with a soccer ball with either a foot or hand, contexts presenting such choices are relatively infrequent.

Duque et al. (2012) showed that repetitive TMS over lateral pFC reduces inhibition associated with CR. This finding would be consistent with the hypothesis that source of CR arises at a fairly abstract level of action representation. Nonetheless, the current results suggest that the manifestation of this form of inhibition is not generic, but rather constrained. We have outlined two factors that could underlie such constraints, one based on anatomical similarity/distance and the other arising from past experience. We note that our experiments are limited to conditions in which the set of response alternatives is rather sparse. Although this may be the case when a decision must be made about how to interact with a single object (e.g., which hand to pick up our coffee cup), response selection is likely to entail much broader forms of competition. Do we pick up the glass to take a sip of wine or the fork to take a bite of dessert? Or perhaps both of these actions are overridden by a desire to respond to our dinner partner. These ideas are amenable to future experimentation, in which the set of response options is expanded, or perhaps more telling, subject to experimental manipulations of experience.

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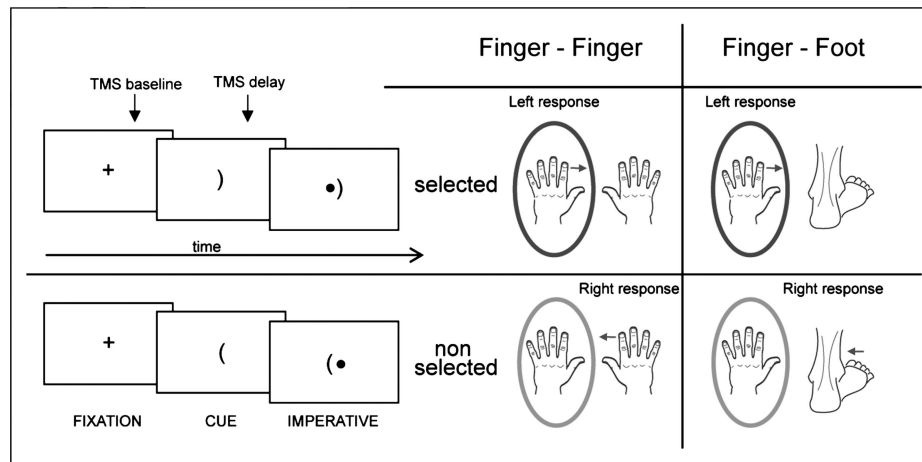


Figure 1.

Sequence of events experimental conditions for Experiment 1. Left: A fixation marker was replaced by a preparatory cue, with the direction of the bracket indicating the forthcoming response. After a 900-msec delay, a circle on the side of the required response served as the imperative signal. A single TMS pulse was applied over right M1 just before the onset of the fixation marker (baseline) or 100 msec before the imperative signal (delay). Right: In separate blocks, the left finger was either paired with the right finger or the right foot. Selected and nonselected refer to the fact that MEPs were always measured in the left FDI.

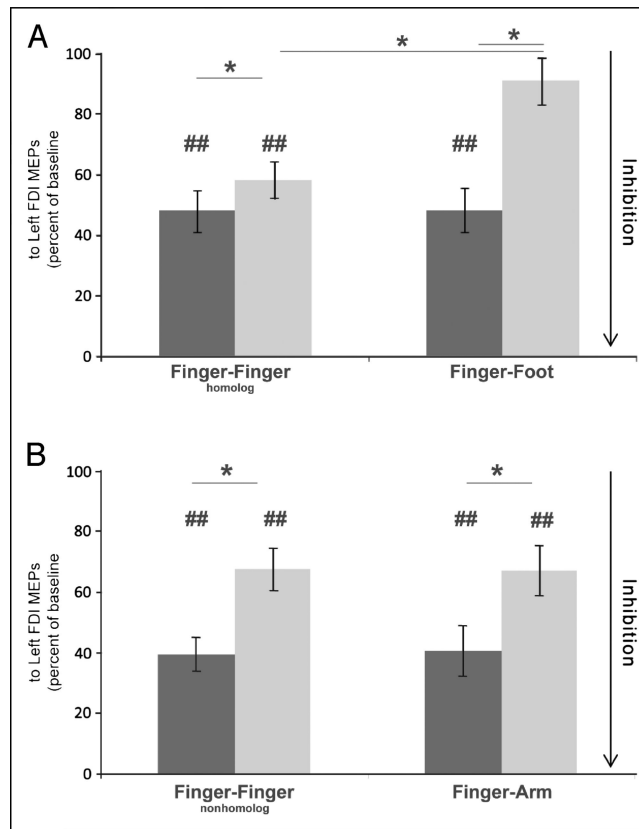


Figure 2.

Modulation of MEPs during the delay period. MEPs recorded from left FDI during the delay period are expressed as a percentage of baseline (100%) for Experiment 1 ($n = 12$, top) and Experiment 2 ($n = 11$, bottom). Dark gray indicates trials in which the left index finger was selected for the forthcoming response. Light gray indicates trials in which the left index finger was not selected. ##Significant reduction of MEP, relative to baseline. *Significant difference in post hoc comparison of linked items. Error bars indicate *SEMs*.

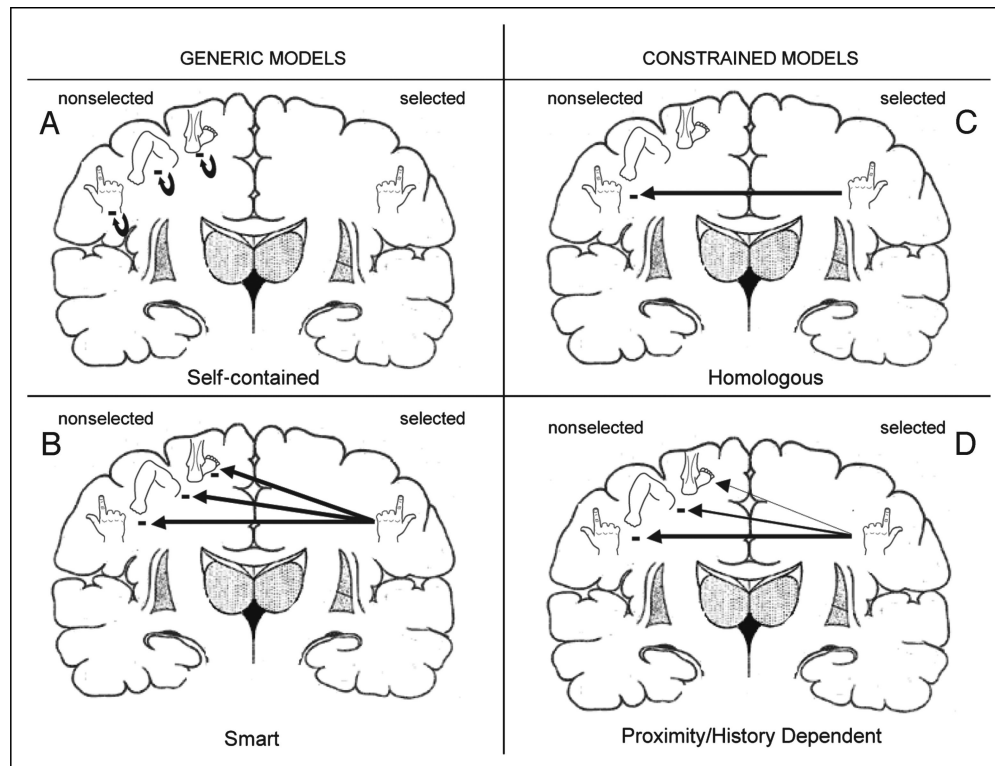


Figure 3.

Four possible architectures for CR. The two models on the left are generic, in the sense that both predict inhibition of the nonselected response for all response pairings. (A) In the Self-contained model, action representations generate self-inhibition when not selected. (B) In the Smart model, a selected action has the capability to inhibit all other task-relevant response representations. The two models on the right predict that the nonselected response will only show inhibition in certain situations (constrained models). (C) The Homologous model assumes that inhibition will be limited to response representations that involve homologous effectors. (D) The Proximity/History Dependent model assumes that inhibition will be graded as a function of response similarity or limited to conditions in which pairs of response representations have been viable alternatives during natural action selection.

Table 1

RTs (msec) for Experiments 1 and 2

Condition	Cue	No TMS	Baseline	Delay
<i>Experiment 1, n = 12</i>				
Finger-Finger _{homolog}	Left	255	236	222
	Right	260	231	226
Finger-Foot	Left	262	240	225
	Right	261	251	223
<i>Experiment 2, n = 11</i>				
Finger-Finger _{nonhomolog}	Left	249	232	227
	Right	226	210	211
Finger-Arm	Left	262	231	211
	Right	262	239	251